The third session on Drug Metabolism and Activity was started by A.H. Beckett (London, England) who dealt with the importance of metabolic studies in drug research and medicine design. He emphasised the importance of detailed metabolic work with drugs for a better understanding of how they act as a basis for the design of new drugs. He referred to his own recent work on the 'hydroxylamines' produced in the body from chlorpromazine and presented in detail the studies on the metabolism of dietylpropion in man.

The session ended with papers by E.J. Ariëns and A.M. Simonis (Nijmegen, The Netherlands) who emphasised that an understanding of the relationship between chemical structure and metabolism was a prerequisite to the development and optimalisation of drugs and by E. Gerhards (Berlin, Germany) who discussed the application of biochemical methods in the pharmaceutical industry.

FOOD AND BULK MATERIALS

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Under the general heading of 'Food and Bulk Materials' separate sessions on carbohydrates (organised by W.J. Whelan) and lipids (organised by L.J. Morris) were held.

In 'Chemistry and Conformation in Polysaccharide Utilisation' D.A. Rees emphasised the extent to which the application of polysaccharides in foods and textiles (and to a lesser extent in a wide variety of industries ranging from explosives to cosmetics) depends on properties for which they were designed by nature. Their use in most industries arose from the empirical approach without any knowledge of the underlying stereochemical principles. The scientific understanding of the latter has already begun to play an ever increasing role in extending the potentialities of both the common (or cheap) carbohydrate sources like starch and cellulose as well as more sophisticated (and expensive) compounds obtained from seaweeds, plant and bacteria. The ribbon-like shape of the cellulose chain and its ability to pack into a structure with strong secondary bonds explain its usefulness in cotton, textiles and paper. The crystalline granule form of natural starch and the changes this undergoes during processing (swelling, dissolution, gel-formation and retrogradation) coupled with variations in the rate and extent of these changes in starches from different plant sources contribute to its use in a wide variety of food industries. The versatility of the native compounds can be dramatically expanded through chemical modification largely involving crosslinking within the molecule. On the other hand nature provides directly a group of heteropolysaccharides whose unique property of gel formation at extremely high dilutions has been exploited for a long time. The mechanisms of gel formation and the relationship between degree of association and the sequence of sugar residues have only recently been studied. Sequence determinations, followed by X-ray analysis, optical rotation studies and circular dichroism spectrum changes on cation binding and gelation have shown that regular sequences give a geometrical fit between chains and are long enough to allow the forces of non-covalent attraction to accumulate to a stable 'bond' that ties the chains together. (junction sites.) A change in covalent sequence (junction terminus) disrupts this regularity and allows separation of the chains until a new association is possible at another site where another sequence of sufficient regularity arises. It is resulting series of chain bundles separated by lengths of unassociated sequences which gives the system its gel character. Chemical modification of the native conformation of polysaccharides of this group enhances the stability of the product and has provided biochemists with the versatile separatory systems used for gel filtration and affinity chromatography.

'The future of Starch and Sucrose in Man's Diet' the paper by J. Yudkin (U.K.) was presented by Dr. Bruckdorfer. Animals and primitive man ate foods best suited to survival but with the advance of civilisation the emphasis changed to elements of palatability and availability. With the emergence of man as a producer, palatability meant foods that have an attractive shape, colour, smell, taste and texture, while availability came to mean those foods, produced com-

mercially and economically. While there is not a taste which is universal, sweetness and a pleasant texture, coupled with the economic facts of agricultural yields, far greater for vegetables than for meat, resulted in a reduction in the protein and fat in man's diet with a considerable increase in carbohydrate. A serious consequence of these changes was evidenced by the many diseases associated with mineral, vitamin and even protein deficiencies.

More recently, with the application of science and technology to all aspects of food production, to plant and animal breeding, agrochemicals, farm mechanisation and food processing, man has further improved his skill and capacity as a food producer. As a result, protein and fat increased and carbohydrate decreased in the diet, but while deficiency diseases decreased it has become apparent that this change was not without health hazards. In the United Kingdom which appears to have reached a 'saturation' level of 50 kilograms per capita per annum, well over half of this is taken in the form of manufactured goods such as jams, biscuits, sweets and soft drinks. It is clear that such an intake, corresponding to approximately one-sixth of the average daily calorie intake, would if taken in addition to a normal diet probably give rise to obesity. If taken instead of an equivalent of other foods it could give rise to, at least mild, deficiency states. Several authorities have expressed disquiet at the poor nutritional value of diets of children and adolescents in the United Kingdom and in the United States, due they believe to the high consumption of sucrose in food and drinks.

While the epidemiological evidence supports the suggestion that sugar intake could be a factor in the development of some of the so called 'diseases of civilisation', namely dental caries, diabetes, peptic ulceration and coronary thrombosis, Yudkin allowed that: 1) sugar intake was not the only dietary concomitant of affluence and 2) other unrelated factors probably contributed to the incidence of these diseases. However, the simultaneous occurrence of two or more of these conditions in the one subject points to a probable common factor in these diseases. Dealing with the experimental evidence for a causative role of sucrose in several diseases, he reported; a) the development of impaired glucose tolerance in human subjects fed large amounts of sucrose (and this in spite of the fact that up to 30% of the subjects showed considerable increase, while none showed a decrease in plasma insulin); b) increased plasma cholesterol and triglyceride and increased platelet adhesiveness in such patients. These factors together with high concentration of insulin have been implicated in atherosclerosis underlying coronary disease; c) the increases in gastric acidity (by 20%) and in pepsin secretion (by 200%) in human volunteers fed high sucrose diets; d) the production in rats, as a result of 'high-sucrose' diets of otherwise unspecified composition a number of 'toxic' effects of such import as to induce the listener to resolve to abstain from sucrose for life! Although the indications are clear, he regretfully concluded that the response will not be vastly different from that generated by the warnings against the deleterious effects of cigarette smoking!

In the third paper on 'The Potential for Starch, Sucrose and Cellulose as Economical Carbon Sources for Industrial Uses' K. Selby (U.K.) pointed to new approaches in which the scientific observations put forward by Rees might be commercially exploited. As a result, the diversion to non-food products of carbohydrate resources, so readily produced using freely available solar irradiation, would help to protect man from the disservice he does himself by his high dietary intake of sucrose, as described by Yudkin. He reviewed current uses and world marked trends of cellulose, starch and sucrose. Cellulose, as cotton, holds over 50% of the textile market and partly because of its own special properties, but also as a result of finishing treatments developed to confer on cotton 'minimum care' properties so advantageous in the synthetic 'cellulosic' fibres, it can be expected to withstand the challenge of the latter over the next decade at least. In a similar manner, and for the same reasons, timber and its major by-product paper are not likely to be surpassed by synthetic substitutes. The chemical reactivity of cellulose has been exploited in the production of a wide variety of modified forms used in the manufacture of explosives, films, paints and plastics. More recently, reports of progress towards the production of single cell protein from cellulose waste products using symbiotic organisms would seem to hold promise of major developments, not only in contributing to the alleviation of the predicted world food shortage by producing edible biomass but also in contributing to a cleaner environment by profitably degrading such waste materials.

The special combination of properties of native

starch and the ease with which these properties could be modified fo. specific purposes have contributed to the highly developed technology surrounding this carbohydrate, and to its place in world markets. Judicious application of etherification and esterification with or without crosslinking can produce modified starches with the varying solubility, viscosity, heat stability, thickening and freezing–thawing properties as required by manufacturers of convenience foods. Modified starches are making their impact on the textile-finishing, paper making and adhesive industries, particularly where the altered characteristic so introduced contributes to the ease and or efficiency of the production line. Future developments must exploit fully the low cost of the basic raw material by developing cheaper processes for manufacturing starch derivatives. This will be of particular importance where increased degrees of substitution are embarked upon in the search for novel properties. In this regard, a process of graft polymerisation, involving relatively high levels of incorporation of monomers such as acrylonitrite, acrylamide and ethylene oxide at present in the early stages of development offer possibilities for selective substitution differing from classical starch chemistry techniques.

The factors contributing to the current high sucrose intake in affluent society, so disturbingly emphasised by Yudkin were highlighted by Selby when he described in detail the properties of sucrose which enhanced the acceptability to the consumer of products in which it was used not only for its sweetness, but also for its contribution to appearance, stability, structure and texture. In many processes, invert sugar produced by acid or enzyme hydrolysis of sucrose has advantages over sucrose itself. The high cost of its production has resulted in the development of interest in a process whereby glucose produced by hydrolysis of starch is then enzymically isomerised to fructose. While some of the fermentation products of sucrose may find their way into the diet, e.g. citric acid, gluconic acid and vitamins, the vast majority of products, various alcohols, organic acids and antibiotics can be considered the true non-food products of the 'sucro–chemical' industry. Other derivatives of which widespread use has been limited largely because of their high cost of production include bio-degradable surfactants, emulsifiers and viscosity modifiers. Here, however, the story is one more of promise than of existing commercial achievement. The extent to which these promises may be realised will, according to Dr. Selby, depend on the development of economic and agricultural policies of industrialised nations and to the ability of research personnel and management of those industries with an interest in the major carbohydrate resources to assess and adapt to the needs of the community and the profitability of their industries.

The second symposium dealt with the application of plant culture technique to breeding and propagation, particularly of oil palm crops (L.H. Jones, U.K.), the present knowledge of the source of and biosynthetic pathways for milk lipids (J.H. Moore, U.K.) and the mechanisms of lipid degradation of foods (C. Eriksson, Sweden).

Utilisable food products are usually the result of specialised metabolism in highly differentiated cells in the plant body. Since such differentiation has not yet been achieved in culture, it is clear that by the use of plant cell cultures the production of bulk food materials is not now, nor in the forseeable future likely to be a viable proposition. In the meantime the techniques that have been developed are being profitably applied in other major areas. The possibility exists for the propagation, via cell culture of oil palms selected (e.g., for high yields, disease resistance and oil quality factors) on the basis of detailed study of embryoids from which plantlets may be regenerated. The recent success in obtaining haploid plants from the culture of immature pollen grains and in achieving diploidisation by variation in the cytokinin content of the medium should allow considerable selection at the pollen grain stage. This could be a useful adjunct to the classical methods in the plant breeder's search for improved crops. A second area of potential for plant culture techniques could be the production of specific and commercially valuable compound lipids, pigments and essential oils. Since many of these are secondary products their production in marketable amounts is incompatible with high yield of biomass. Making optimistic assumptions as regard to performance for a hypothetical plant product it was clearly shown that plant cell cultures might be of commercial value for valuable materials required in small quantities only. Knowledge of the biosynthetic pathway might allow the induction of specific secondary product synthesis. Unpublished work by Macrae and How on rose cultures was used to illustrate this point and to define the

formidable problems still to be overcome. The uniformity of plant cell cultures provides an ideal system for the study of general metabolic pathways as exemplified by the studies at Unilever on the desaturase system in fatty acid biosynthesis. In particular such cultures allow the study of control mechanisms in biosynthetic pathways without the limitations imposed by the transient nature of many components observed in greenhouse grown-plants.

'Lipid Biochemistry – from forage to milk' by J.H. Moore was a detailed presentation of the pathways of biosynthesis of the lipid components of bovine milk. Phospholipids from herbage, and triglycerides from food concentrates are hydrolysed, and unsaturated fatty acids hydrogenated by rumen microorganisms, which in addition carry out de novo synthesis of their own cellular lipids. The source of hydrogen for the hydrogenation of mono- and di-enoic fatty acids is not known; there are conflicting reports about the extent of hydrogenation of poly-enoic acids. The main lipid components of the material passing through the omasum and abomasum into the small intestine are the non-esterified fatty acids adsorbed to particulate matter. Adsorption of these probably arises through micellar formation facilitated by the bile salts and by the lysophosphatidyl choline derived from biliary phosphatidyl choline. Triglyceride synthesis in the intestinal mucosa then proceeds via the phosphatidic acid pathway and produces a thoracic duct lymph with composition analogous to that in non-ruminants. Although little is known about the composition, biosynthesis and metabolism of bovine serum lipoproteins it is clear that they differ markedly from the widely studied human lipoproteins. While the concept was proposed over 30 years ago that ruminant milk fatty acids are derived both from blood lipids and from de novo synthesis in mammary gland, the development of reliable methods of lipid analysis has now led to detailed investigations of the pathways involved. No uptake of sterols, sterol esters or phospholipids by mammary gland could be detected, whereas large uptake of triglycerides and of acetate from the blood were observed. Acetate was incorporated into fatty acids from 4:0–16:0, but much of the milk fat 16:0 and all of the 18:0 and 18:1 were derived directly from plasma triglyceride through the probable intervention of capillary endothelial lipoprotein lipase. The de novo synthesis of milk fatty acids appears to occur predominantly in the cytosol by the malonyl-co A pathway, but the mechanism of chain termination responsible for the characteristic short and medium chain fatty acids has not been elucidated. Evidence from studies on rabbit mammary tissue suggests that this is under hormonal control. Failure to demonstrate incorporation of acetate into C.18 fatty acid suggests that the bovine mammary gland has lost the mitochondrial and microsomal fatty acid elongation systems. The carbon utilised for de novo synthesis is derived almost entirely from blood acetate and β-hydroxy butyrate; the apparent absence of the citrate cleavage pathway from ruminant tissues would explain why glucose carbon is not available for fatty acid synthesis. Finally while both the phosphatidic acid and 2-monoglyceride pathways operate in ruminant mammary gland, the weight of evidence supports the former as the major pathway for the synthesis of milk triglycerides. It seems likely that the glycerol-3-phosphate component is derived from plasma glucose taken up by the gland. Some, at least, of the glycerol may be derived from the action of lipoprotein lipase; this could then undergo phosphorylation by glycerokinase which has been shown to be present in the tissue. Stereospecific analysis of crow's triglycerides indicate that their 1,2-diglyceride cores are derived from a common pool of 1,2-diglycerides in mammary tissue and that the synthesis of low and high molecular weight triglyceride is completed by esterification in position 3 with short and long chain fatty acid, respectively.

In 'Enzymic and Non-Enzymic Lipid Degradation in Foods' C. Eriksson (Sweden) discussed the mechanisms of oxidation of unsaturated fatty acids to produce aldehydes, the presence of which could be beneficial or detrimental depending on their concentration, composition and the type of foodstuff in which they occur. In most cases, however the accumulation of aldehydes in food gives rise to rancidity; in many vegetables and fruits alcohol dehydrogenase may reduce these aldehydes to the corresponding alcohols. Precise information concerning these reactions and reaction products would be of value in the understanding of their contribution to flavour. The oxidative step has been attributed to two elements, the enzyme, lipoxygenase and the non-enzymic action of haematin compounds. From studies on the catalytic activity of these agents and that of alcohol dehydrogenase in fresh,

heat treated and frozen vegetables specific problems in quality control in this field can be defined and biochemical approaches to their solution proposed. Thermal preservation procedures designed to inactivate the enzymes have been shown to increase the catalytic effect of the haemoproteins. This effect is due to increased exposure of the haeme groups towards the lipid substrate. Thus, the products of lipid degradation in a particular 'preserved' vegetable will vary from the fresh state, according to whether it is frozen or dried in the blanched or unbalanced condition. Knowledge about the exact mechanism of oxygen transfer, the source of the superoxide anion O_2^- and the role of superoxide dismutase may help to provide new means of controlling both the initial oxidation and the subsequent reduction reactions. Results reported for aldehyde–alcohol equilibria point to the possibility of controlling that aspect of food flavour ascribed to the presence of these compounds. Evidence was also presented to show how a detailed study of the cellular localisation of the lipids, the catalysts and the naturally occurring antioxidants might explain the rapid onset of lipid degradation as soon as natural conditions cease.

ANALYTICAL TECHNIQUES

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Two topics were the main concerns of this symposium: Analytical techniques used in quality control and the automation of biochemical analyses.

In her talk on quality controls in biochemical production Dr. Grassl of Boehringer (Mannheim) emphasised the need for analyses at all stages of the manufacturing procedure. Although the outlined control scheme appeared to be complex, experience had shown the necessity for this thorough testing. Without it a commercial concern could not control its costs and hence its profits.

Two laboratories were responsible for these analyses. The control laboratory was responsible for the testing of incoming raw materials, analysis of finished products and control testing of the final packaged goods before shipment. In-process analyses were the responsibility of the production department.

A notable feature of the control laboratory's work was testing of incoming raw materials. All material, not merely source material, was tested. Analyses of glass bottles and stoppers, for example, consisted of inspection for appearance and cleanliness, measurements of strain, determination of inorganic contaminants and size measurement. Extraction with perchloric acid was a notably useful method for assessing contamination.

The in-process analyses during biochemical production were of the type totally familiar to biochemists. Enzymes, substrates and co-enzymes were measured by activity and possibly specific activity. Measurement at every purification stage was economically essential. Absolute specificity of the assay was not required at this stage and of course interference often occurred in crude fractions. However, with controlled incoming raw materials satisfactory reproducibility with different batches was an indication of process performance.

After production, the finished products returned to the Control Laboratory for objective assessment. Total activity and specific activities were precisely measured. The specificity and accuracy of the testing methods were particularly important here and examples of individual assays of glucose-6-phosphate dehydrogenase and trypsin were presented in some detail. The other important parameter of the finished biochemical product was its stability. It was interesting to learn that amounts of stabilizers (e.g. sugar, glycerol and ammonium sulphate) can be critical and are individual to each enzyme.

In this discussion of quality control the analyses used were of the manual type familiar to all laboratory workers. The remaining talks in the symposium were concerned with easing the burden of repetitive manual analyses. The requirement for this automation in an industrial situation was not made apparent by any of the speakers. The examples of automated analyses were talks from the field of clinical analysis. The need for a